

Appl. No. 10/748,192
Amendment dated: March 24, 2009
Reply to OA of: December 24, 2008

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1(original). A temperature-sensitive thermogelling emulsion delivery system, comprising:

a biodegradable temperature-sensitive aqueous phase polymer solution;

at least one bioactive substance, and

a pharmaceutically acceptable oil phase carrier, said oil carrier embeds said bioactive substance;

wherein

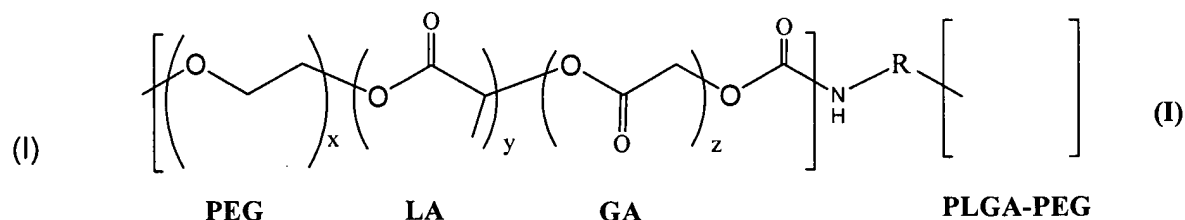
said oil phase carrier and said temperature-sensitive polymer solution are mixed mutually to form an emulsion, which is a liquid while at a temperature below a lower critical solution temperature (LCST) and transforms into a gel while the temperature of the emulsion is above said lower critical solution temperature (LCST).

2(original). The delivery system as claimed in claim 1, wherein said bioactive substance is embedded in said oil phase carrier by the means of dissolving, solid suspension or water/oil emulsification.

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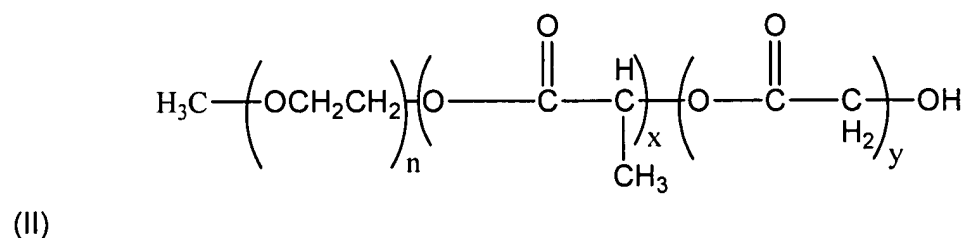
3(currently amended). The delivery system as claimed in claim 1, wherein said temperature-sensitive polymer is selected from the group consisting of poly(ethylene glycol (PEG)-poly(lactic acid-co-glycolic acid) (PLGA)-PEG ~~PEG-PLGA-PEG~~, ~~PLGA-PEG-PLGA~~, ~~PEG-PLGA~~ and Poloxamer ~~Poloxamer~~ 407.

4(currently amended). The delivery system as claimed in claim 3, wherein said poly(ethylene glycol(PEG)-poly(lactic acid-co-glycolic acid)(PLGA)-PEG ~~PEG-PLGA-PEG~~ is represented as formula (I):



wherein x is a positive integer between 5 to 20; y is a positive integer between 20 to 40; z is a positive integer between 5 to 20; and R is the substituted linear or branched C₂ to C₁₀ alkyl group.

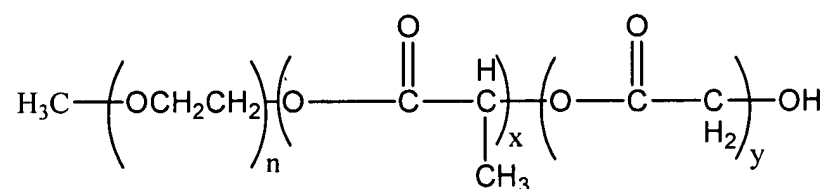
5(original). The delivery system as claimed in claim 3, wherein said PEG-PLGA is represented as formula (II):



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wherein n is a positive integer between 5 to 20; x is a positive integer between 20 to 40; and y is a positive integer between 5 to 20.

6(original). The delivery system as claimed in claim 3, wherein said Poloxamer 407 is represented below:



7(original). The delivery system as claimed in claim 1, wherein said physiologically accepted oil phase carrier is a fatty acid ester.

8(currently amended). The delivery system as claimed in claim 7, wherein said physiologically accepted oil phase carrier is selected from the group consisting of a fatty acid ester lipiodol, medium chain triglyceride (MCT), soybean oil, sesame oil, castor oil, sunflower oil, mineral oil, vitamin E oil or a mixture of them.

9(original). The delivery system as claimed in claim 1, wherein at least one bioactive substance is selected from the group consisting of chemical compound, protein, peptide, nucleic acid, polysaccharide, carbohydrate, lipid, glycoprotein and imaging agent.

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10(previously presented). The delivery system as claimed in claim 1, in a form for subcutaneous injection, intramuscular injection, intratumor injection or embolism agent.

11(previously presented). The delivery system as claimed in claim 1 which is a liquid while at a temperature below a lower critical solution temperature (LCST) which is from 23-27°C and transforms into a gel while the temperature of the emulsion is above 30°C.

12(previously presented). The delivery system as claimed in claim 3 which is a sustained release drug delivery system and which is a liquid while at a temperature below a lower critical solution temperature (LCST) which is from 23-27 °C and transforms into a gel while the temperature of the emulsion is above 30°C.

13(currently amended). The delivery system as claimed in claim 7, wherein said physiologically accepted oil phase carrier is selected from the group consisting of fatty acid ester lipiodol, medium chain triglyceride (MCT), soybean oil, sesame oil, castor oil, sunflower oil, mineral oil, vitamin E oil or a mixture thereof and wherein at least one bioactive substance is selected from the group consisting of chemical compound, protein, peptide, nucleic acid, polysaccharide, carbohydrate, lipid,

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glycoprotein and imaging agent.

14(currently amended). The delivery system as claimed in claim 12, wherein said physiologically accepted oil phase carrier is selected from the group consisting of fatty acid ester ~~lipid~~, medium chain triglyceride (MCT), soybean oil, sesame oil, castor oil, sunflower oil, mineral oil, vitamin E oil or a mixture thereof and wherein at least one bioactive substance is selected from the group consisting of chemical compound, protein, peptide, nucleic acid, polysaccharide, carbohydrate, lipid, glycoprotein and imaging agent.

15(new). A temperature-sensitive thermogelling emulsion delivery system, comprising:

a biodegradable temperature-sensitive aqueous phase polymer solution comprising a polymer selected from the group consisting of PEG-PLGA-PEG, PLGA-PEG-PLGA, PEG-PLGA and Poloxamer 407;

at least one bioactive substance, and

a pharmaceutically acceptable oil phase carrier selected from the group consisting of fatty acid ester, medium chain triglyceride (MCT), soybean oil, sesame oil, castor oil, sunflower oil, mineral oil, vitamin E oil, and a mixture thereof, and wherein said oil carrier embeds said bioactive substance in a form of soluble in oil, solid-in-oil, water-in-oil, or a mixture thereof; and

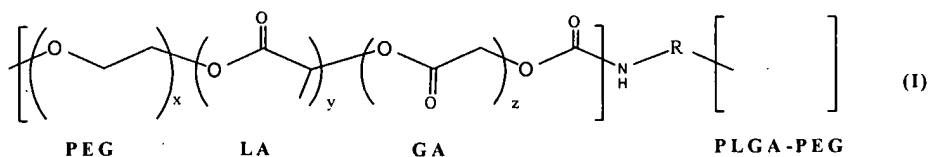
wherein said oil phase carrier and said temperature-sensitive polymer solution

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are in mixed with each other in the form of an emulsion, which is a liquid while at a temperature below a lower critical solution temperature (LCST) and transforms into a gel while the temperature of the emulsion is above said lower critical solution temperature (LCST).

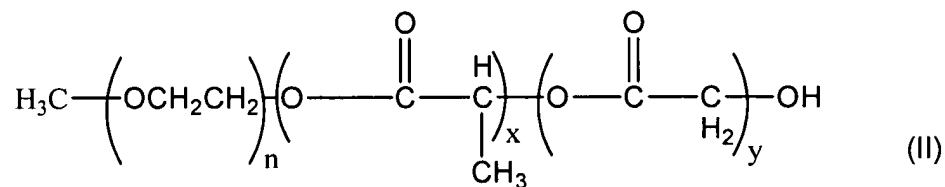
16(new). The delivery system as claimed in claim 15, wherein said bioactive substance is embedded in said oil phase carrier by means of dissolving, solid suspension or water/oil emulsification.

17(new). The delivery system as claimed in claim 15, wherein said PEG-PLGA-PEG is represented as formula (I):



wherein x is a positive integer between 5 to 20; y is a positive integer between 20 to 40; z is a positive integer between 5 to 20; and R is the substituted linear or branched C₂ to C₁₀ alkyl group, and

said PEG-PLGA is represented as formula (II):



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wherein n is a positive integer between 5 to 20; x is a positive integer between 20 to 40; and y is a positive integer between 5 to 20.

18(new). A temperature-sensitive thermogelling emulsion delivery system, comprising:

a biodegradable temperature-sensitive aqueous phase polymer solution comprising a polymer selected from the group consisting of PEG-PLGA-PEG, PLGA-PEG-PLGA, PEG-PLGA and Poloxamer 407;

at least one bioactive substance, and

a pharmaceutically acceptable oil phase carrier, wherein said oil carrier embeds said bioactive substance in a form of soluble in oil, solid-in-oil, water-in-oil, or a mixture thereof; and

wherein said oil phase carrier and said temperature-sensitive polymer solution are mixed to form an emulsion, which is a liquid while at a temperature below a lower critical solution temperature (LCST) and transforms into a gel while the temperature of the emulsion is above said lower critical solution temperature (LCST), and

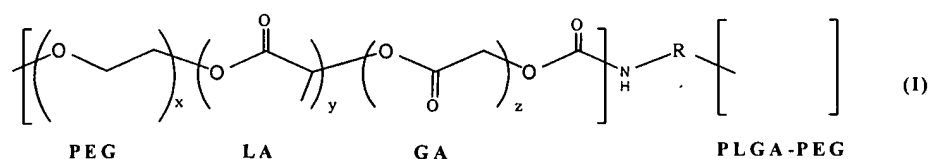
wherein said temperature-sensitive thermogelling emulsion delivery system provides a 3-10 fold greater sustained release of said bioactive substance as compared to a hydrogel as measured by a test comprising adding 0.2 ml of said emulsion or hydrogel in a Release Cell by placing said emulsion or hydrogel on a

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Thermostate Module, maintaining said emulsion or hydrogel for 10 minutes at $37.0 \pm 1.0^\circ\text{C}$, setting a sieve and stirring bar for five minutes, adding 5ml of preheated Release Medium by stirring of 100 rpm to activate the release effect, and measuring said sustained release effect.

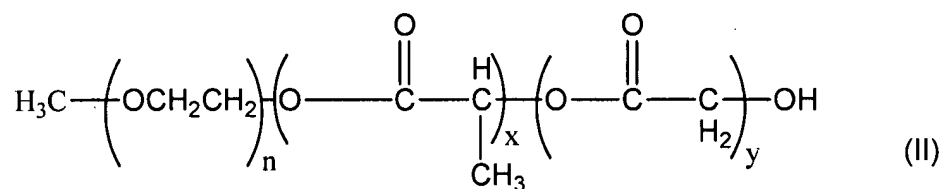
19(new). The delivery system as claimed in claim 18, in a form for subcutaneous injection, intramuscular injection, intratumor injection or embolism agent.

20(new). The delivery system as claimed in claim 18, wherein said PEG-PLGA-PEG is represented as formula (I):



wherein x is a positive integer between 5 to 20; y is a positive integer between 20 to 40; z is a positive integer between 5 to 20; and R is the substituted linear or branched C_2 to C_{10} alkyl group, and

said PEG-PLGA is represented as formula (II):



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wherein n is a positive integer between 5 to 20; x is a positive integer between 20 to 40; and y is a positive integer between 5 to 20.